

Impact of covid 19 manifestation on thyroid function status in previously euthyroid patients: A cross sectional study

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ABSTRACT

Background: A new coronavirus (severe acute respiratory syndrome coronavirus 2; SARS-CoV-2) infection began to spread in China, in early December 2019 and has rapidly spread around the globe. While its effects on respiratory symptoms are well recognized, but its effect on thyroid function test is still unclear. We initiated this study with the aim of comparison of thyroid function of Covid-19 affected individuals with that of unaffected individuals. **Methods:** Clinical examination, laboratory investigation and computed tomography study (CT severity score) of 50 patients with RT-PCR confirmed covid-19 infection who were tested for thyroid function test during their course of hospitalization in covid positive ward in the department of medicine. Other 50 individual who were admitted in covid negative section of the hospital with acute respiratory symptoms during the same period and were found RTPCR negative were also included in the study as control group. Thyroid profile of these two groups were analysed and compared to each other. **Result:** During the course of COVID-19, of the patients with COVID-19, 74% (37/50) had more-than normal TSH levels, with a p value of < 0.001. As compared with non-COVID-19 pneumonia patients with the serum TSH levels of the patients with COVID-19 were significantly higher. **Conclusion:** This supports the effects of SARS-Cov2 on Thyroid gland, thus proving the postulate that COVID19 may be inducing hypothyroidism which is majorly subclinical. None of the patients received thyroid hormone replacement therapy during the course of our study.

Keywords: covid 19, thyroid profile, euthyroid, subclinical thyroiditis.



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1. INTRODUCTION

The outbreak of corona virus disease caused by a new strain known as severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2) has spread throughout the world and was declared a pandemic by WHO in March 2020 (Jabaris et al., 2021). The first case of covid 19 infection in India was reported on January 30th in the state of Kerala. Until now the virus has infected 17,997,267 cases in India and caused 201,187 deaths.

The effects covid 19 on lungs and immune system are well recognised, there are still lack of studies explaining the effects of virus on thyroid gland and thyroid function. Few studies only highlighted the thyroid function association in covid 19 patients till now. Thyroid is a major gland of the endocrine system affecting the basal metabolic rate of our body (Talwar et al., 2020). Hence the aim of the study is to see the changes of thyroid function in covid infection by comparing the thyroid function of covid affected patients with that of Non covid patients.

2. METHOD

This cross sectional study was conducted at department of medicine, Jawaharlal Nehru medical college, Wardha between June 2020 to June 2021. Amongst all the covid 19 patients, 50 patients were examined for thyroid function test during their stay in the hospital. Patients with previous history of thyroid diseases and ongoing pregnancy were not considered for the study. The thyroid function test of these 50 patients included of 3 parameters which was serum total thyroxine (TT4), total triiodothyronine (TT3) and thyroid stimulating hormone (TSH), reference range of which are (5.53 to 11 mcg/dl), (0.97 to 1.96 ng/ml) and (0.46 to 4.68 mcg/dl) respectively. All the 3 parameters of the thyroid function test were performed using chemiluminescent assay. Non COVID affected patients who presented with acute respiratory symptoms similar to those of COVID-19 but were found to be RT-PCR negative and with HRCT showing no evidence of COVID-19 pneumonia or HRCT findings of respiratory diseases other than that of COVID-19 pneumonia were admitted in the COVID negative section of the hospital during the similar period who also underwent test for thyroid function were included in the study as control group. This control group of 50 individuals were age matched to that of case group and had no previous history of thyroid disease or ongoing pregnancy. The thyroid function test i.e TT3, TT4 and TSH levels were then compared between the COVID-19 case and control group.

Statistical analysis

Statistical analysis was done by using descriptive and inferential statistics using chisquare test, Odd's Ratio and Pearson's Correlation Coefficient and software used in the analysis were SPSS 24.0 version and GraphPad Prism 7.0 version and $p < 0.05$ is considered as level of significance.

3. RESULTS

Among patients ($n = 50$), mean age of the patients were 49.98 ± 15.80 , male being 54% and female 46%, shown in table 1. Out of 50 cases 6 (12%) had high TT3, 24 (48%) had low TT3; whereas in control, 9(18%) patients had high TT3, 14(28%) had low TT3 ($p = 0.039$ s) as shown in table 2 and represented in figure 1. Out of 50 cases 13 (26%) had high TT4, 15 (30%) had low TT4; whereas in control, 15(30%) patients had high TT4, 14(28%) had low TT4 ($p = 0.65$ s) as shown in table 3 and represented in figure 2.

Table 1 Age and Gender wise distribution of patients in two groups

Age Group (yrs)	Cases n=50	Controls n=50
18-40 yrs	17(34%)	17(34%)
41-60 yrs	21(42%)	21(42%)
>60	12(24%)	12(24%)
Mean \pm SD	48.98 \pm 15.80	48.08 \pm
Range	22-78 yrs	21-80
Gender		
Male	27(54%)	27(54%)
Female	23(46%)	23(46%)

Table 2 Distribution of patients in two groups according to TT3

TT3	Cases (n=50)	Controls (n=50)	χ^2 -value
Normal	20(40%)	27(54%)	4.24 p=0.039,S OR=2.37 (95% CI=1.03- 5.44)
HIGH TT3	6(12%)	9(18%)	
Low TT3	24(48%)	14(28%)	
Total	50(100%)	50(100%)	
Mean \pm SD(ng/ml)	2.22 \pm 1.58	1.44 \pm 0.55	
Range	0.36-8.56	0.03-3.03	

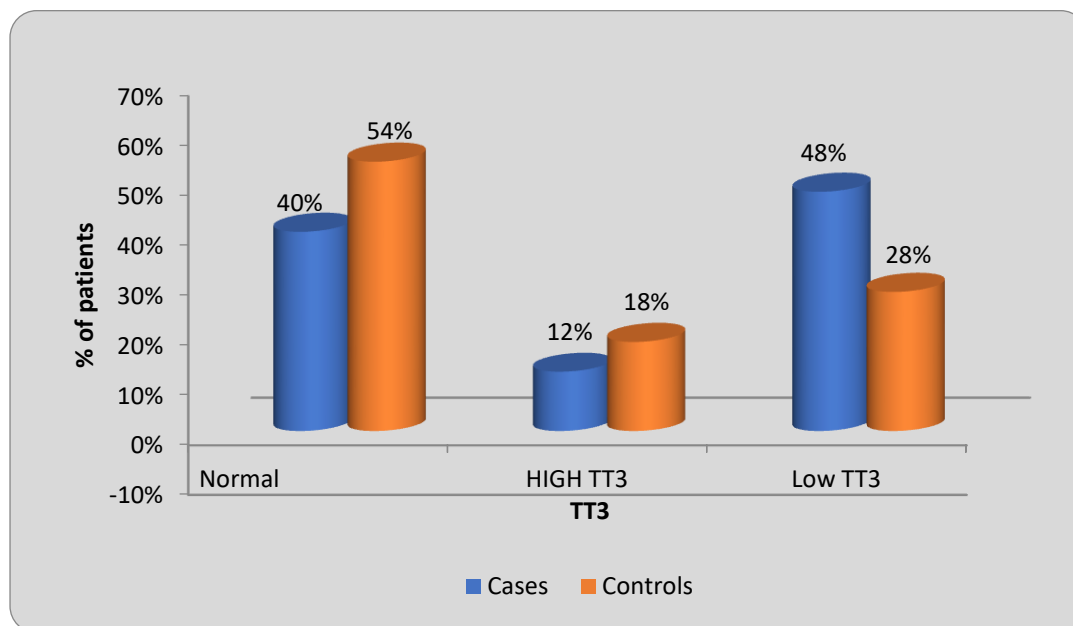
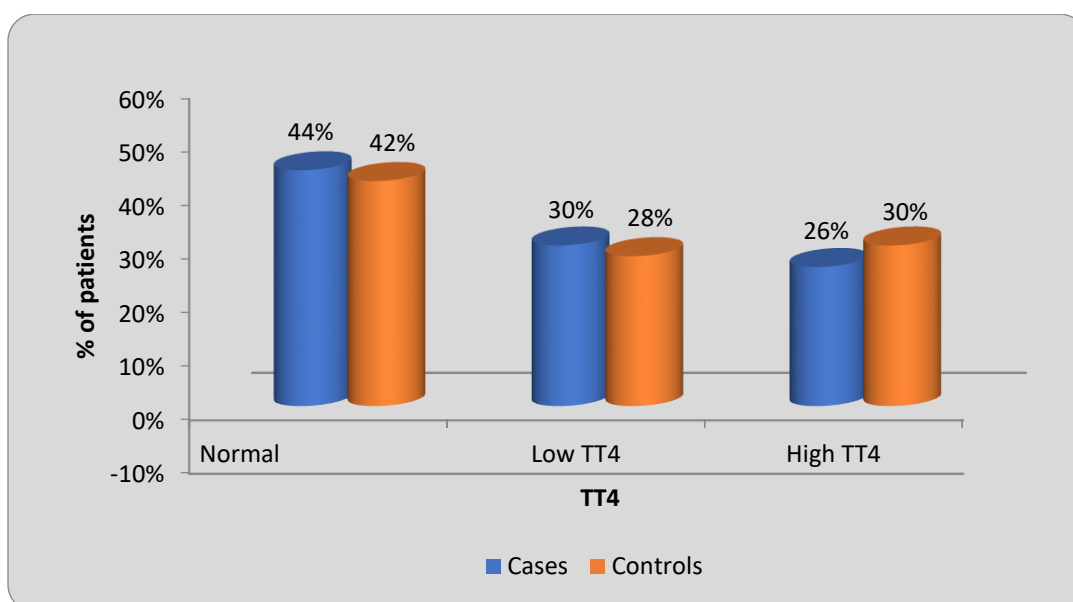
**Figure 1** Showing representation of normal, high and low TT3 between cases and control group.**Figure 2** Showing representation of normal, high and low TT4 between cases and control group.

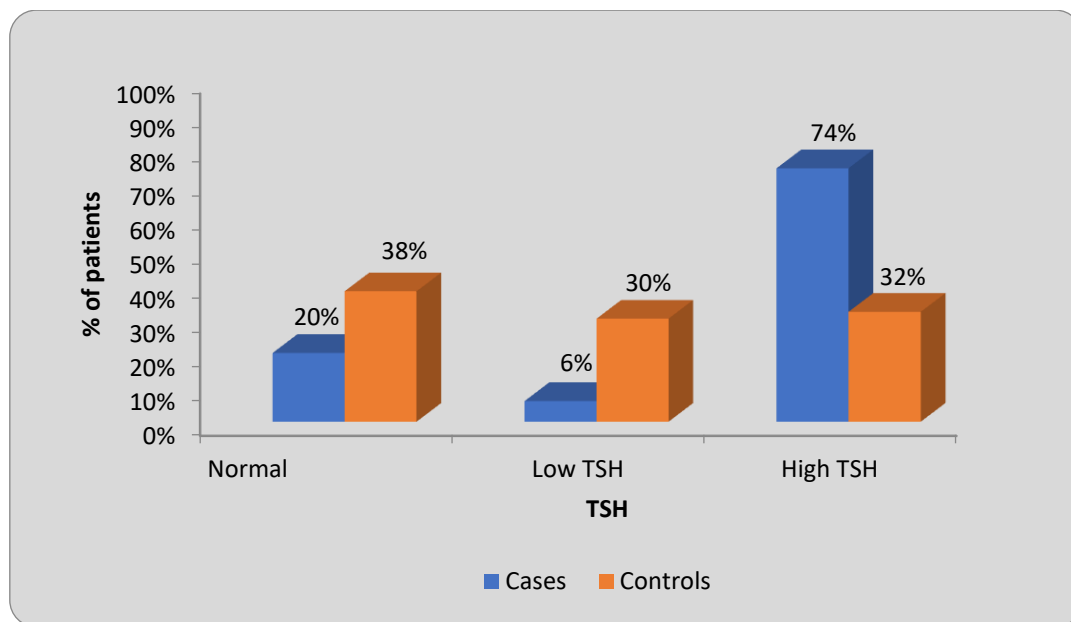
Table 3 Distribution of patients in two groups according to TT4

TT4	Cases (n=50)	Controls (n=50)	χ^2 -value
Normal	22(44%)	21(42%)	0.19 p=0.65,NS OR=1.22 (95% CI=0.50- 2.92)
Low TT4	15(30%)	14(28%)	
High TT4	13(26%)	15(30%)	
Total	50(100%)	50(100%)	
Mean \pm SD	7.12 \pm 2.90	7.28 \pm 2.77	
Range	1-15	1.43-12.17	

Out of 50 cases 37 (74%) had high TSH, 3(6%) had low TSH; whereas in control, 16(32%) patients had high TSH, 15(30%) had low TSH (p= 0.0001 s) as shown in table 4 and figure 3.

Table 4 Distribution of patients in two groups according to TSH

TSH	Cases (n=50)	Controls (n=50)	χ^2 -value
Normal	10(20%)	19(38%)	17.70 p=0.0001,S OR=0.16 (95% CI=0.06-0.39)
Low TSH	3(6%)	15(30%)	
High TSH	37(74%)	16(32%)	
Total	50(100%)	50(100%)	
Mean \pm SD	1.12 \pm 1.63	2.86 \pm 2.46	
Range	0.02-5.34	0.11-9.75	


Figure 3 Showing representation of normal, high and low TSH between cases and control group.

4. DISCUSSION

Ever Since it's breakout in 2019, COVID19 has proved to be a multisystem disease which effects not only the respiratory system but has paramount importance in multisystem dysfunction. Endocrine system regulated the normal functioning of our body however thyroid gland is the most important gland of endocrine system (Khoo et al., 2021). Serious disease effecting the thyroid gland results in disorder which is known as nonthyroidal illness syndrome or euthyroid sick syndrome. It is emerging to be a big difficulty to treat thyroid disorders caused by COVID19 as it is a neglected field of domain in the ongoing exhausting pandemic. Common

abnormality witnessed in COVID19 as far as thyroid gland is concerned is Low T3, Normal T4 and Raised TSH (Giovannella et al., 2021). This forms a picture of Hypothyroidism in a previously euthyroid patient.

During the course of hospital stay the patients with COVID-19, 74% (37/50) had More-than normal TSH and 48% (24/50) had less than normal TT3 levels, with a p value of < 0.001 and < 0.039 respectively. TT4 was not much different between COVID-19 and non-COVID-19. TT3 was found to be on the lower side in patients tested positive for COVID19 as compared to control. This supports the effects of SARS-Cov2 on Thyroid gland, thus proving the postulate that COVID19 may be inducing hypothyroidism which is majorly subclinical (Sen et al., 2020). Hypothyroidism even when sub clinical is important to detect to prevent further complications (Beralkar et al., 2018). None of the patients received thyroid hormone replacement therapy during the course of our study. Thyroid disorders can range from an excess of thyroid hormones known as hyperthyroid and deficiency of thyroid hormone known as hypothyroid state (Dubey et al., 2018).

Our study focuses on Hypothyroid encountered as a result of COVID19. Hypothyroidism can be illustrated by a high TSH and Low serum T3 or T4 (Acharya et al., 2014). It is important to note that none of our patients were receiving hormone replacement therapies and were diagnosed as a case of Hypothyroidism for the first time during their COVID19 disease course. It is postulated that there is significant injury to the follicular and parafollicular cells of the thyroid gland by SARS-CoV2 similar to what was witnessed by the old SARS outbreak (Wei et al., 2007). This injury might be the pathophysiology behind the subclinical hypothyroidism manifesting in COVID19. Anterior Pituitary plays a vital role in regulation of thyroid hormone cycle. It is found that the TSH secreting cells of anterior pituitary are also effected by COVID19 which might be linked to increased TSH levels found in our cases.

There might be direct effect of the SARS-Cov2 on the thyroid producing cells of the thyroid gland or the proinflammatory cytokines secreted during the cytokine storm of COVID19 might exert inflammatory effects on the thyroid cells leading to hypothyroidism. We thus warrant the investigation for Thyroid profile in patients presenting with COVID19 as it might be a subclinical disease waiting by the corner for a adverse manifestation such as myxedema coma or hypothyroid periodic paralysis.

Limitation

shortcomings of our study was that free T3, free T4, and other pituitary hormones were not assessed at the time of admission due to the retrospective nature of the study. In addition, thyroid function of the patients after there full recovery could not be assessed due to difficult follow up of these patients owing to nation wide lockdown. As our hospital is a tertiary care, we admitted only moderate to sever COVID-19 cases due to which effect of thyroid function on mild cases who were mostly home quarantined could not be studied.

5. CONCLUSION

After studying the data of 50 cases and 50 controls we concluded that changes in serum TSH and thyroid hormone levels may be important manifestations of moderate to sever cases of COVID-19.

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We thank the participants who were all contributed samples to the study.

Author Contributions

PJ, SK, SA was involved in the concept and design of the study as well as in the writing of the manuscript. SB, DT, CB, GJ, RD supervised the development of work while PV, MP, SK collected the data and performed data analysis. All authors read and approved the final manuscript.

Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Ethical approval

The study was approved by the Medical Ethics Committee of Datta Meghe Institute of Medical Sciences Deemed to be University (ethical approval code: DMIMS(DU)/IEC/2021/336).

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Declaration of conflicting interests

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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